

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (Currently amended). A vector for delivery of a virus to a target cell within a host animal, ~~comprising~~ consisting essentially of a cell-targeting ligand non-covalently bound directly to said virus,
wherein said ligand binds directly to a receptor on said target cell.

Claim 2. (Original) The vector of claim 1 wherein said virus and said ligand are not naturally associated with each other.

Claim 3. (Original) The vector of claim 1, wherein said virus is comprised of a therapeutic nucleic acid.

Claim 4. (Original) The vector of claim 1, wherein said virus is comprised of a nucleic acid that encodes a therapeutic peptide or protein.

Claim 5. (Original) The vector of claim 1, wherein said virus is comprised of a nucleic acid that encodes wild-type p53.

Claim 6. (Original) The vector of claim 1, wherein said virus is a retrovirus or an adenovirus.

Claim 7. (Original) The vector of claim 1, wherein said virus is selected from the group consisting of adeno-associated virus, herpes simplex virus, cytomegalovirus, vaccinia virus, fowlpox virus, canarypox virus and Sindbis virus.

Claim 8. (Original) The vector of claim 1, wherein said virus is a chimeric virus, a hybrid virus, or a recombinant virus.

Claim 9. (Original) The vector of claim 1, wherein said cell-targeting ligand is selected from the group consisting of proteins, peptides, hormones, antibodies and antibody fragments.

Claim 10. (Original) The vector of claim 1, wherein said cell-targeting ligand is a native protein or a recombinant protein.

Claim 11. (Original) The vector of claim 1, wherein said cell-targeting ligand is selected from the group consisting of insulin, toxins, EGF, VEGF, FGF, IGF, heregulin, a viral protein, a bacterial protein, estrogen and progesterone.

Claim 12. (Original) The vector of claim 1, wherein said cell-targeting ligand is transferrin.

Claim 13. (Original) The vector of claim 1, wherein said cell-targeting ligand and said virus are present at a ratio in the range of 100 to 1,000,000 ligand molecules per virion.

Claim 14. (Original) The vector of claim 1, wherein said cell-targeting ligand and said virus are present at a ratio in the range of 6,700 to 400,000 ligand molecules per virion.

Claim 15. (Original) The vector of claim 1, wherein said cell-targeting ligand and said virus are present at a ratio in the range of 1 μ g to 10 mg of said ligand per 10^{10} virion.

Claim 16. (Original) The vector of claim 1, wherein said cell-targeting ligand and said virus are present at a ratio in the range of 10 μ g to 600 μ g of said ligand per 10^{10} virion.

Claim 17 (Currently amended). A method for preparing a vector for the systemic delivery of a virus to a target cell, said vector ~~comprising~~ consisting essentially of a cell-targeting ligand non-covalently bound directly to said virus, comprising mixing said cell-targeting ligand with said virus in an aqueous medium, whereby said ligand non-covalently binds directly to said virus.

Claim 18. (Original) The method of claim 17, wherein said aqueous solution includes one or more of a buffering agent, an osmolarity adjusting agent, or an antibiotic.

Claim 19. (Currently amended). A method for targeting delivery of providing a nucleic acid ~~therapeutic agent~~ to cancer cells of an animal suffering from head and neck cancer, bladder cancer, breast cancer, thyroid cancer, ovarian cancer, prostate

cancer, melanoma or lymphoma, comprising administering systemically to said animal ~~a therapeutically effective amount of a viral vector for delivery of a virus comprising said therapeutic agent consisting essentially of a virus comprising said nucleic acid to cells of one of said cancers within said animal, said vector comprising and a cell-targeting ligand which is non-covalently bound directly to said virus and binds directly to a receptor which is over-expressed on said cells containing a receptor for said ligand.~~

Claim 20. (Original) The method of claim 19, wherein said animal is human.

Claim 21. (Canceled)

Claim 22. (Original) The method of claim 19 wherein said therapeutic agent is administered parenterally.

Claim 23. (Original) The method of claim 19 wherein said therapeutic agent is administered intravenously or intra-arterially.

Claim 24. (Canceled).

Claim 25. (Currently amended) The method of claim 19, 39, 40 or 41 wherein said vector encodes wild-type p53.

Claim 26. (Currently amended) The method of claim 19, 39, 40 or 41 wherein said cell-targeting ligand is transferrin.

Claim 27. (Original) The method of claim 19 wherein said therapeutic agent is administered to an animal receiving chemotherapy in addition to said therapeutic agent.

Claim 28. (Original) The method of claim 19 wherein said therapeutic agent is administered to an animal receiving radiation treatment in addition to said therapeutic agent.

Claim 29. (Currently amended). The method of claim 19, 39, 40 or 41 wherein said virus is comprised of a nucleic acid encoding wild-type p53 and said cell-targeting ligand is transferrin ~~and said therapeutic agent is administered systemically.~~

Claim 30. (Canceled)

Claim 31. (Canceled)

Claim 32. (Original) The vector of claim 1, wherein said virus is an adenovirus comprising a therapeutic nucleic acid and said ligand is transferrin or EGF.

Claim 33. (Original) The vector of claim 1, wherein said virus is an adenovirus and said ligand as an antibody fragment.

Claim 34. (Original) The vector of claim 33, wherein said adenovirus comprises a nucleic acid that encodes wild-type p53.

Claim 35. (Original) The vector of claim 34, wherein said adenovirus comprises a nucleic acid that encodes wild-type p53.

Claim 36. (Original) The vector of claim 1, wherein said virus is a retrovirus or herpes simplex virus comprising a therapeutic nucleic acid and said ligand is transferrin.

Claim 37. (Original) The method of claim 19, wherein said virus is an adenovirus, a retrovirus or a herpes simplex virus.

Claim 38. (Currently amended) The method of claim 30, 37 wherein said virus is an adenovirus.

Claim 39. (New) A method of specifically targeting and sensitizing cancer cells to radiation or chemotherapy which comprises systemically administering to a person suffering from cancer a viral vector complex consisting essentially of an admixture of (1) a virus comprising a nucleic acid which will sensitize said target cells to radiation or chemotherapy and (2) a targeting ligand which is bound directly and non-covalently to said virus and will bind directly to said cancer cells such that said nucleic acid is delivered to said cancer cells; wherein said cancer cells are selected from head and neck cancer, bladder cancer, breast cancer, thyroid cancer, ovarian cancer, prostate cancer, melanoma or lymphoma, and said cancer cells overexpress a receptor for said ligand.

Claim 40. (New) A method of increasing the levels of expression of a nucleic acid of interest in target cancer cells, which comprises systemically administering an effective amount of

a viral vector complex which consists essentially of a virus comprising said nucleic acid and a ligand which is bound directly and non-covalently to said virus and binds directly to a receptor overexpressed on said target cancer cells; wherein expression of said nucleic acid of interest in said target cancer cells sensitizes said cells to radiation or chemotherapy; and further wherein said target cancer cells are selected from the group consisting of head and neck cancer, bladder cancer, breast cancer, thyroid cancer, ovarian cancer, prostate cancer, melanoma and lymphoma.

41. (New) In a method of administering a chemotherapeutic or radiation therapy agent to an animal suffering from head and neck cancer, bladder cancer, breast cancer, thyroid cancer, ovarian cancer, prostate cancer, melanoma and lymphoma the improvement which comprises

systemically administering to said animal prior to said chemotherapy or radiation a viral vector complex which consists essentially of (1) a virus comprising a nucleic acid which when expressed in cancer cells sensitizes said cells to radiation or chemotherapy and (2) a ligand which is bound directly to a receptor on said virus and bind directly to a receptor on said cancer cells.

Claim 42. (New) A method of specifically targeting and sensitizing cancer cells to radiation or chemotherapy which comprises administering intratumorally to a person suffering from cancer a viral vector complex consisting essentially of an admixture of (1) a virus comprising a nucleic acid which will sensitize said target cells to radiation or chemotherapy and (2) a targeting ligand which is bound directly and non-covalently to said virus and will bind directly to said cancer cells such that said nucleic acid is delivered to said cancer cells; wherein said cancer cells are selected from head and neck cancer, bladder cancer, breast cancer, thyroid cancer, ovarian cancer, prostate cancer, melanoma or lymphoma, and said cancer cells overexpress a receptor for said ligand.

Claim 43. (New) A method of increasing the levels of expression of a nucleic acid of interest in target cancer cells, which comprises administering intratumorally an effective amount of a viral vector complex which consists essentially of a virus comprising said nucleic acid and a ligand which is bound directly and non-covalently to said virus and binds directly to a receptor overexpressed on said target cancer cells; wherein expression of said nucleic acid of interest in said target cancer cells sensitizes said cells to radiation or chemotherapy; and further wherein said target cancer cells are

selected from the group consisting of head and neck cancer, bladder cancer, breast cancer, thyroid cancer, ovarian cancer, prostate cancer, melanoma and lymphoma.

44. (New) In a method of administering a chemotherapeutic or radiation therapy agent to an animal suffering from head and neck cancer, bladder cancer, breast cancer, thyroid cancer, ovarian cancer, prostate cancer, melanoma and lymphoma the improvement which comprises

administering intratumorally to said animal prior to said chemotherapy or radiation a viral vector complex which consists essentially of (1) a virus comprising a nucleic acid which when expressed in cancer cells sensitizes said cells to radiation or chemotherapy and (2) a ligand which is bound directly to a receptor on said virus and bind directly to a receptor on said cancer cells.